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L1: Entry 1 of 1 File: USPT May 1, 2001

DOCUMENT-IDENTIFIER: US 6225525 B1
TITLE: ATP-binding cassette transporter (ABC1) modified transgenic mice

DEPR:
ABC1 knockout mice that survive to be weaned appear to develop normally and mature into apparently healthy adults. Between 4-6 months of age the mice of both lines begin to develop respiratory distress and shed granular casts into their urine. Necropsy examination reveals lungs heavily filled with blood and cardiomegaly with dilated hypertrophied left and right ventricles. There is occasional evidence of vasculitis around the cardiac vessels. The kidneys are pale tan in color. Microscopic examination reveals boxcar nuclei in the heart consistent with cardiac hypertrophy with frank pulmonary hemorrhages as well as severe congestion of the lungs, liver and spleen, and scarred kidney glomeruli. The glomeruli show evidence of inflammatory infiltrates, thickened and "split" glomerular basement membranes and proliferation of mesangial cells. Scarring of glomeruli was visible when sections were stained with trichrome (FIG. 4A). Immunohistochemistry confirms the deposition of both Ig and C3 complement components in the glomeruli characteristic of membranoproliferative glomerulonephritis type I (FIG. 4B). To summarize, in knockout ABC1 mice we find evidence of immune complex and complement deposition in kidney glomeruli, inflammation, glomeruli nephritis, cardiomegaly and congestive heart failure.

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L5: Entry 2 of 3 File: USPT Apr 4, 2000

DOCUMENT-IDENTIFIER: US 6046035 A
TITLE: Polynucleotides encoding a cardiotrophin-like cytokine

BSPR:
Cardiotrophin-1, or CT-1, is the member of the IL-6 cytokine family most closely related by sequence identity to the amino acid sequence of the gene of the present invention. CT-1 was identified by combining an expression cloning approach with an embryonic stem cell-based model of in vitro cardiogenesis (Sheng, Z., et al., Development 122:419-428; 1996; Pennica, D., et al., Proc. Natl. Acad. Sci. USA 92:1142-1146; 1995; Ishikawa, M., et al., Biochim. Biophys. Res. Comm. 219:377-381; 1996). Adult cardiac muscle is terminally differentiated and, unlike skeletal muscle, cardiac muscle tissue does not contain muscle cells which retain their proliferative capacity. As a result, injury to the heart muscle is often irreversible and results in scarring and ultimately in an overall decrease in heart function.

DEPR:
The determined nucleotide sequence of the CLC cDNA of FIGS. 1A and 1B (SEQ ID NO:1) contains an open reading frame encoding a protein of 225 amino acid residues, with an initiation codon at nucleotide positions 46-48 of the nucleotide sequence in FIG. 1A (SEQ ID NO:1), and a deduced molecular weight of about 25.2 kDa. The amino acid sequence of the CLC protein shown in SEQ ID NO:2 is about 29.0% identical and 47.8% similar to rat cardiotrophin-1 mRNA (FIG. 2; Ishikawa, M., et al., Biochem. Biophys. Res. Commun. 219:377-381; 1996; GenBank Accession No. D7859 1). The homology between CT-1 and CLC indicates that CLC may be involved in similar physiological roles.